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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,770	01/08/2002	Yi Hu	LEX-0294-USA	3157

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EXAMINER
SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
1652	6

DATE MAILED: 08/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	10/041,770	HU ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a well established utility for either the nucleic acid molecule of SEQ ID NO: 1 or any nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2. Furthermore, the claimed invention is not supported by an asserted utility based on either a demonstrated function for the protein of SEQ ID NO: 2, or by a deduced function for said protein supported by homology to known proteins.

The asserted utility for the protein of SEQ ID NO: 2, based on shared structural similarity, is as a metalloprotease (p2 lines 5-9). Sequence searches showed no consistent homology for the protein of SEQ ID NO: 2 with metalloproteases. In addition, the protein of SEQ ID NO: 2 does not contain the conserved His-Glu-Xxx-Xxx-His-Xxx-Xxx-His motif of the catalytic domain (Fahrenholz et al, 2000) or the Prro-Arg-Cys-Gly-Xxx-Pro motif of the propeptide domain (Massova et al, 1998) of metalloproteases. Thus, the identity of the polynucleotide sequence of SEQ ID NO: 1, or any other polynucleotide sequence encoding the protein of SEQ ID NO: 2, as encoding a metalloprotease is not credible.

As stated in the specification, the proposed utilities for SEQ ID NO: 1 are: microarrays, or other assay, to screen genetic material from patients; identification of mutations associated with SEQ ID NO: 1; diagnostic assays; preparation of anti-sense oligonucleotides derived from SEQ ID NO: 1; hybridization assays; library screening; characterization of genomic clones;

PCR; restriction fragment length polymorphism analysis; isolation of full-length cDNA; preparation of fusion proteins; preparation of antibodies; as therapeutics (page 8-16); analysis of protein evolution; and preparation of transgenic animals (page 17-19). Each of these utilities is an application which would apply to every member of a general class of materials and/or is a use only for further research to determine a use for SEQ ID NO: 1 or the protein encoded thereby. As such, these asserted utilities are not specific (for those applicable to all human DNAs) or not substantial because the use of SEQ ID NO: 1 therein is only potential and not in currently available in practical form. Therefore, Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by an established utility.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2 is indefinite in the recitation of "hybridize" as this term is unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids which, will hybridize under some hybridization conditions, will not necessarily hybridize under different conditions. Claim 2 claims an isolated nucleic acid molecule that encodes SEQ ID NO: 2 and hybridizes under highly stringent conditions to SEQ ID NO: 1 or the complement thereof. The specification reads:... "under highly stringent conditions e.g., hybridization to filter-bound DNA in 0.5M NaHpO4, 7% SDS, 1mM EDTA at 65°C, and washing in 0.1x SSC/0.1% SDS at 68°C". Because the description for highly stringent conditions is exemplary and not defining,

Claim s is rendered indefinite. See MPEP § 2173.05(d). Therefore, Claim 2 is rejected under 35 U.S.C. 112, second paragraph, for failing to distinctly claim the subject matter of the invention.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a demonstrated, deduced, or well established function for the protein of SEQ ID NO: 2, or encoded by SEQ ID NO: 1, for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1 and 4 are also rejected under 35 U.S.C. 112, first paragraph, because even if the specification were enabling for the nucleotide sequence of SEQ ID NO: 1 or any nucleotide sequence that encodes the protein of SEQ ID NO: 2, reasonable enablement for any nucleotide sequence comprising at least 60 contiguous nucleotides of SEQ ID NO: 1 would not be provided. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1 and 4 are so broad as to encompass any polynucleotide sequence that comprises at least 60 contiguous nucleotides of SEQ ID NO: 1. The scope of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a

knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen multiple substituted or truncated proteins or polynucleotides , as encompassed by the instant claims, and the regions within a protein's sequence that can be modified and/or deleted with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable.

The specification does not support the broad scope of the Claims 1 which, encompasses any polynucleotide sequence that comprises at least 60 contiguous nucleotides of SEQ ID NO: 1. The specification also does not support the broad scope of Claim 4 which, encompasses any vector comprising said polynucleotide sequences. The specification does not support the broad scope of Claims 1 and 4 because the specification does not establish: (A) regions of the polynucleotide and encoded protein structure which may be modified and/or deleted without effecting the activity of the encoded peptide; (B) the general tolerance of the activity of the encoded peptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying and/or deleting any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of nucleotide sequences that comprises at least 60

contiguous nucleotides of SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1 and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of nucleic acid molecules comprising at least 60 contiguous nucleotides from SEQ ID NO: 1.

The specification does not contain any disclosure of the function of all DNA sequences that comprise at least 60 contiguous nucleotides from SEQ ID NO: 1. This genus of nucleic acid molecules is a large variable genus with the potentiality of encoding many different activities. Therefore, many functionally unrelated nucleic acid molecules are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus, SEQ ID NO: 1, for which the asserted utility is not credible; thus, the disclosure is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Fujiwara et al, 1996 or NCI-CGAP, 1999. Fujiwara et al, and NCI-CGAP each teach polynucleotide sequences comprising at least 60 contiguous nucleotides from SEQ ID NO: 1. The polynucleotides taught by Fujiwara et al and NCI-CGAP are: GenBank Acc #D78761 and #AI637480, respectively. Since Claims 1 and 4 claim isolated nucleic acid molecules comprising at least 60 contiguous nucleotides from SEQ ID NO: 1, Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Fujiwara et al, 1996 or NCI-CGAP, 1999.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 8:30-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600